A COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF DIFFERENT SCHEDULES OF ADAPTATION TO HYPOXIA

P.V. Vasil'ev, V.B. Malkin, F.V. Babchinskiy, Ye.V.Loginova, N.A. Roshchina and G.D. Yukhnovskiy

ABSTRACT: Research was carried out on white mice and rats. Based on data from changes in the animals' weight, the number of erythrocytes, the amount of hemoglobin, oxygen requirements and survival of mice at high altitudes, we can give a comparative evaluation of the natural - high-altitude and pressure-chamber adaptations (prolonged continuous adaptation for 30 days at an altitude of 2000 and 3800 m, continuous brief adaptation for 3 days, adaptation at an altitude of 3000 - 7000 m; interrupted adaptation of daily stay at " high altitude" for 6 hours for a period of 2 weeks at "altitudes" of 3000 - 7000m). It was established that the adaptation effect, found as a result of animals remaining at high altitudes and in a pressure chamber at these same "altitudes" and with the same exposure, does not change appreciably. Under pressure-chamber conditions it makes sense to set up schedules for which the adaptation is carried out with a gradual increase in altitude up to relatively high values with a significant variation in the barometric pressure during the course of the days.

The creation of scientifically based schedules of adaptation for man and animals to conditions of lowered barometric pressure has great practical significance both for aviation and space medicine as well as for occupational and athletic physiology.

In developing such schedules it is natural that we should attempt to insure that a sufficiently high and sufficiently maintained adaptation effect be obtained for a minimally short period of time. In spite of the importance of this question it has been studied very little. All concepts concerning a schedule of carrying out adaptation to conditions of lowered barometric pressure have an empirical nature. Here, of value is the experiment on mountain climbing where certain common positions concerning a rational sceduale of adaptation were confirmed. The most widely used schedules in mountain climbing obtained were those which provide for a gradual ascent to high altitude and allow a periodic descent from it. /123

The purpose of this research was a comparative evaluation of the effectiveness of adaptation to factors of altitude which occur under natural mountain conditions and with various schedules of

pressure-chamber conditioning. To solve this problem we first of all required that we choose criteria which would permit judging as to the effectiveness of the adaptation. As we know from the literature data there is no single concept concerning this problem.

Since the center of attention of our research was a study of the possibilities and the feasibility of using adaptation to hypoxia as a means for increasing the tolerance of an organism to different extreme factors we chose as the basic sign of the effectiveness of adaptation the tolerance of animals to acute oxygen insufficiency.

In the experiments on animals we studied and compared the effectiveness of adaptation attained with continuous stay under conditions of lowered barometric pressure (mountains and pressure-chamber), with a daily residence for a period of 6 hours in a pressure chamber at "altitudes" which were gradually raised from 3500 to 7000 m (interrupted adaptation) and with continuous residence for a period of the same time at the same altitude.

METHOD

We made three series of experiments in which we used 1000 white mice and 50 white rats.

In the first series a comparative evaluation was given of the effect obtained with natural, high-altitude and continuous pressure-chamber adaptation of the animals. Here in the pressure chamber the degree of evacuation of air ("altitude") and the duration of residence in it were the same as in the mountains.

The adaptation of animals to hypoxia was carried out both at high altitude regions of Mount Elbrus at an altitude of 2000 m above sea level (Terskol) for 18 days and at an altitude of 3800 m (Ledovaya Baza) for 12 days and under pressure-chamber conditions at the same altitude and with the same exposure. In the pressure chamber in all series of experiments the humor and the carbonic acid excreted by the animals was absorbed by chemical absorbants /124
(KhPI and silica gel). Along with this the chamber was periodically ventilated as a result of which fixed conditions were maintained in it: a relative humidity of 55-85%, a temperature of 20-24°, a carbon dioxide content which did not exceed 1%. To retain these conditions service personnel entered the pressure chamber through a transfer chamber.

The control animals were chosen from the same group as the experimental animals. They were kept under conditions of the vivarium in Moscow using the same system of supply as the experimental animals.

The effectiveness and the duration of retention of adaptation to lowered barometric pressure were determined basically according to the survival of animals during ascent in the pressure chamber to

an altitude of 9000 m (rate of ascent 80-100 m/sec), with exposure in it in one series of 3-4 minutes and in the others until all of the animals died.

In the latter case the lifetime of each animal was taken into account.

From the literature data it is known that increasing the altitude promotes a more rapid development of adaptation. In this respect in the second series of experiments we determined the possibility of shortening the times of adaptation at the expense of increasing the "altitude" of ascent. Thus we investigated the possibility of obtaining a high adaptation effect for a shorter period of time.

In the second and third seried of experiments we carried out those in which the overall duration of the effect of hypoxia was shortened to 78 hours but the "altitude" was significantly increased at which the adaptation took place. In this case we studied two schedules of conditioning: a continuous gradula conditioning in the process of which the animals were placed into a pressure chamber for a period of 78 hours with a gradual increase in "altitude" and an interrupted conditioning when the total length of time in the pressure chanber was also 78 hours but the entire adaptation process was extended to 13 days. The schedule of the continuous gradual and interrupted pressure-chamber adaptations is shown on Table 1.

TABLE 1. TIME OF CONTINUOUS GRADUAL AND INTERRUPTED PRESSURE-CHAMBER ADAPTATION.

Altitude, m	Continuous, hours	Interrupted, days (6 hrs each day)	Altitude, m	Continuous, hours	Interrupted, days (6 hrs each day)
3000	6	1	5500	6	7
4000	12	2 and 3	6000	6	8
4500	6	4	6500	12	9 and 10
5000	12	5 and 6	7000	18	11 and 13

The third series of experiments was carried out for comparison /125
of the effects obtained during continuous and interrupted adaptation to altitude under pressure-chamber conditions.

With interrupted adaptation the daily residence in the pressure chamber was 6 hours $\pm$ 20 minutes.

In these series of experiments along with the tolerance of the mice to acute hypoxia for different periods of time after end of exposure we also investigated changes in the red blood of the rats.

RESULTS

In the first series of experiments it was established that the tolerance to acute oxygen starvation of mice after remaining in mountains at altitudes of 2000 to 3800 m and at the same altitudes under pressure-chamber conditions is increased almost to the same degree. In this case the adaptation effect disappears after 12-14 days following descent from "high altitude". In the animals who were apapted under natural conditions a negative phase was detected. We made our judgment concerning this on the basis that the tolerance of the experimental animals to acute hypoxia after 14 days was found to be lower than the tolerance of the control animals. After the 16-18th day in the experimental animals the altitude tolerance was again reduced and remained practically the same as in the control animals.

As was shown above for a clearer explanation of the role of "altitude" in the adaptation effect in the second series of experiments we carried out a comparative evaluation of tolerance to acute hypoxia after remaining in the mountains (maximum altitude 3800 m) and an interrupted pressure-chamber adaptation (maximum altitude 7000 m).

In the first four days after completion of the natural and the pressure-chamber adaptations the tolerance to hypoxia of both groups of mice was similar. The slight predominance of the adaptation effect in the mice placed under pressure-chamber conditions may apparently be due to the fact that they were tested in the first days following completion of adaptation whereas the animals who were in the mountains were tested somewhat later, on the fourth day following descent from high altitude (Table 2).

In the mice who were adapted to altitude under pressure-chamber conditions the increased tolerance to acute hypoxia was retained for 18-20 days.

The adaptation effect following residence in the mountains by the 14th day faded, after which the animals even attained a slightly increased tolerance to acute hypoxia.

Consequently the daily residence for 6 hours of animals in the pressure chamber with a gradual increase in altitude (for 2 weeks from 3000-7000 m) led to an increase in their tolerance to acute hypoxia. Here the adaptation effect was retained for a longer period of time than after a 30-day continuous residence in mountains or in a pressure chamber at lower altitudes (2000-3800 m).

It has already been shown that in rats the changes in red blood were studied both in the process of natural and in pressure-chamber adaptations. In animals who were at an altitude of 2000 m above sea level practically no changes were observed in the red blood The residence of rats at an altitude of 3800 m under high-altitude

TABLE 2. SURVIVAL OF MICE (IN %) AT AN ALTITUDE OF 9000 m FOR DIFFERENT PERIODS OF TIME FOLLOWING DESCENT FROM THE MOUNTAINS AND INTERRUPTED PRESSURE CHAMBER ADAPTATION. /126

Group of Animals	Time after end of adaptation, days					
	4	14	16	18	20	22
Pressure chamber, altitude 3000-7000 m	75	60	55	55	55	35
Control	5	0	0	25	30	40
P	>0.01	>0.01	>0.01	unreliable		
Mountains, altitude 2000-3800 m	85	45	35	30		
Control	35	40	55	30		
P	>0.01		unreliable			

conditions accompanied by an increase in the amount of erythrocytes on an average to one million (15%). After interrupted pressure-chamber adaptation the number of erythrocytes in the peripheral blood increased on the average to two million (30%).

Both residence in mountains and daily 6-hour conditioning of animals in the pressure chamber produced an increase in hemoglobin that was similar in value, from 14-15 to 16.5-17.5 gram %.

After residence in mountains the amount of red blood was normalized for a period of 4-7 days. After conditioning in the pressure chamber the increased amount of erythrocytes and hemoglobin was retained for a period of 7-9 days; only by the 14th day did the amount of hemoglobin and erythrocytes reach a normal level.

Thus continuous residence in a pressure chamber, simulating mountains only in the degree of evacuation of air, permitted us to obtain an adaptation effect that was near to that obtained in animals under high-altitude conditions.

With interrupted pressure-chamber adaptation when the time of action on the organism by the hypoxic factor was decreased but its force was increased the time of retention of the adaptation reactions of the red blood and the increased tolerance to acute hypoxia esceeded the time of retention of the effect following residence in mountains by almost 2 times, at the relatively low altitudes of 2000-3800 m.

Consequently, under pressure-chamber conitions, apparently /127
it makes sense to use schedules of adaptation which provide for a gradual ascent to high altitudes.

Research is known in which an adverse effect has been noted on the organism of animals from a periodic ascent in a pressure chamber

to different altitudes [1].

If we analyze the conditions of the above experiments and compare them with the results of investigations by us and by other authors who have found a positive effect, we can make the assumption that the negative results obtained by these authors are due to unsuccessful schedules of adaptation.

If we assume that the adaptation effect is determined only by the time and the force of the hypoxic factor then continuous residence of animals in a pressure chamber at the same altitudes and for the same period of time as with interrupted adaptation (see Table 1) would have to give a similar effect and shorten the total time spent in conditioning to a considerable degree (Table 3).

TABLE 3. LIFETIME OF MICE (IN MINUTES) AT HIGH ALTITUDE FOR DIFFERENT PERIODS OF TIME FOLLOWING CONTINUOUS AND INTERRUPTED RESIDENCE IN A PRESSURE CHAMBER.

Group	Time after end of adaptation, days					
	1	6	9	14	19	22
After continuous adaptation	13.3	15.2	11.1	7.1	3.3	1.9
Control	11.1	6.3	1.9	7.2	2.6	7.0
P	<0.5	>0.5	>0.01	<0.5	<0.5	<0.5
After interrupted adaptation	26.2	3.9	13.9	3.8	3.5	
Control	7.2	2.6	7	2.7	3.8	
P	>0.01	>0.01	>0.5	<0.5	<0.5	

The duration of retention of the adaptation effect following interrupted and continuous pressure-chamber adaptations was almost the same. Howe er, altitude tolerance of animals following interrupted adaptation was found to be considerably higher than the tolerance to acute hypoxia of animals who remained continuously at "high altitude" in the pressure chamber.

Just as in the previous series, changes in the tolerance of animals to acute hypoxia after interrupted adaptation had a clearly expressed wave-shaped character. The shorter period of time of retention of altitude tolerance in this series of experiments in comparison with the previous ones we are inclined to attribute to seasonal factors.

As has been shown, the increase in the number of erythrocytes /128 and the amount of hemoglobin in the animals after remaining in the pressure chamber as a rule was retained for a period of 7-9 days.

On the second day followning completion of the three-day continuous adaptation the number of erythrocytes on the average exceed- the number of erythrocytes of the control group by 400,000, by the

sixth-seventh days a considerable increase was noted in the number of erythrocytes (to 1-1.5 million) with a subsequent decrease to the original values. Changes in the amount of hemoglobin were not associated with changes in the number of erythrocytes: on the second day following completion of the adaptation the increase in hemoglobin was more significant, by the sixth day the amount of hemoglobin was decreased to the original level and then remained in this range.

In this series of experiments the blood was taken also from mice. Interrupted pressure-chamber adaptation produced a gradual significant increase in the number of erythrocytes on the average from 7,700,000 to 11,500,000 and a rapid decrease in their number after cessation of the effect of "altitude" too8,290,000 by the eighth day. Such a large increase in the number of erythrocytes was accompanied also by an increase in the amount of hemoglobin.

The dynamics of changes in the red blood in mice with continuous adaptation we e found to be to a significant degree similar to changes of red blood in the rats.

Thus in spite of the equal period of time and the strength of the effect of the hypoxic factor in these two series of experiments there are nevertheless significant distinctions both in the increased altitude tolerance obtained as a result of adaptat on and in changes in the red blood. Apparently for the process of adaptation large fluctuations in the barometric pressure throughout the days has significance.

CONCLUSIONS

1. The adaptation effects obtained as a result of residence of animals in the mountains (2000 and 3700 m) and in the pressure chamber at the same "altitudes" and for the same period of time do not differ substantially.

2. Under pressure-chamber conditions it makes sense to create schedules for which the adaptation is carried out with a gradual in crease in altitude up to relatively high values and with significant fluctuations in barometric pressure throughout the period.

3. The high effectiveness of an "interrupted" conditioning schedule in the pressure chamber gives a basis for its practical utilization both for keeping the previously attained adaptation and to produce the primary effect.

REFERENCES

1. Armstrong, H.I. and I.W. Heim: Aviat. Med., No. 9, p. 92, 1938. /129
2. Regnolds, O.: Amer. J. Physiol. No. 150, p. 65, 1947.
3. Atland, P.D. and B.J. Highman: Aviat. Med., No. 28, p. 253, 1956.
4. Atland, P.D. and B.J. Highman: Aviat. Med., No. 168, p. 345, 1952.